

## **II. REMARKS**

### **I. Status of the Claims**

Claims 1-101 were filed with the original application. Claims 26-101 were cancelled pursuant to a restriction requirement. Claims 1-25 were pending and rejected by the final Office Action dated April 7, 2004 (“Action”). Claim 1 is amended. Support for this amendment can be found on page 9, lines 28-30. Claims 24 and 25 have been amended to be consistent with claim 1. The amendments place the case in better condition for allowance and would not involve a new search.

Claims 1-25 are the subject of this response.

### **II. Claims 1-25 Are Enabled under 35 U.S.C. § 112, First Paragraph**

Claims 1-25 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention. The Action argues that because the prior art disclosed that some normal tissues, including intestinal epithelium, and tissues under stress can express MICA, mere detection of MICA and/or MICB is “insufficient as an indicator of cancer in the sample or the subject from whom the sample was obtained.” Action at page 3. It concludes that the claimed invention is not enabled because it does not provide a means for differentiating cancerous samples from normal tissue or noncancerous stressed tissue. Applicants respectfully traverse.

Claim 1 had been amended to recite a method for screening for “potential carcinogenesis” in a patient to emphasize the diagnostic aspect of the invention and to highlight that individual diagnostic methods used by clinicians are not foolproof. Often, a diagnostic method or screen indicates a patient possibly has a particular disease or condition, which—

depending on the disease or condition—allows the clinician to act accordingly. In some cases, subsequent tests are conducted to further support a diagnosis or a treatment option is initiated based on that diagnosis, which may or may not be 100% accurate or conclusive (such as when antibiotics are given for pneumonia, even though the disease may have a viral origin). Accordingly, the present claims reflect that methods of the invention screen for “potential carcinogenesis.”

The examiner relies upon two references to support his argument that MICA and/or MICB is expressed in normal and noncancerous stressed tissue. Both of these papers show expression of MICA and/or MICB only in one tissue—intestinal epithelial cells—and not in any other tissue. The reference of Groh *et al.*, *Science* 279:1737-1740, 1998, describes data obtained from intestinal epithelial cell lines, while the reference of Groh *et al.*, *PNAS* 93:12445-12450, 1996, identifies MICA and MICB expression in gastrointestinal epithelium. The authors of this latter paper reported no expression in brain, heart, lung, thyroid, liver, kidney, skin, adrenal glands, placenta, tonsil, and spleen.

However, this does not mean the claims are not enabled. Even if claims read on nonoperative subject matter, the claims can be enabled. *Atlas Powder Co. v. E.I. duPont de Nemours*, 750 F.2d 1569, 1577 (Fed. Cir. 1984). “It is not a function of the claims to specifically exclude . . . possible inoperative substances. . . .” *Id.* In this case, as the examiner admits, the prior art already teaches the skilled artisan that one tissue expresses MICA and MICB. The identification of a single nonoperative embodiment by the prior art does not render the claims as lacking enablement. A person of ordinary skill in the art would still be able to practice the claimed invention because they would know 1) the source of the sample being tested according to the method of the invention; and, 2) that expression of MICA and/or MICB where it would not

normally be observed was a *potential* indication of carcinogenesis. The skilled person would, therefore, have a context for practicing the invention. Accordingly, it would not require undue experimentation to perform the claimed methods of the invention.

Thus, Applicants respectfully submit that the examiner has not advanced a *prima facie* case of non-enablement, and if advanced, applicants have provided sufficient rebuttal evidence to establish that MICA and MICB can, in fact, be used as the basis for cancer diagnosis. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

### **III. Conclusion**

Applicants submit that, in light of the foregoing, all claims are in condition for allowance, and an early notification to that effect is earnestly solicited. Should the examiner have any questions regarding this response, a telephone call to the undersigned is invited.

Respectfully submitted,



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